Reply Dated July 23, 2003

Reply to Office Action of December 30, 2002

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Amended) A compound of formula I in which

$$R^{5}$$
 R^{6}
 R^{7}
 R^{3}

A stands for the group = NR^2 ,

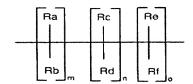
W stands for oxygen, sulfur, two hydrogen atoms or the

group =NR⁸,

Z stands for the group $=NR^{\dagger \theta}$ or =N-,

-N(\mathbb{R}^{10})-($\mathbb{C}H_2$) $_q$ -, branched or unbranched \mathbb{C}_{1-0} alkyl or

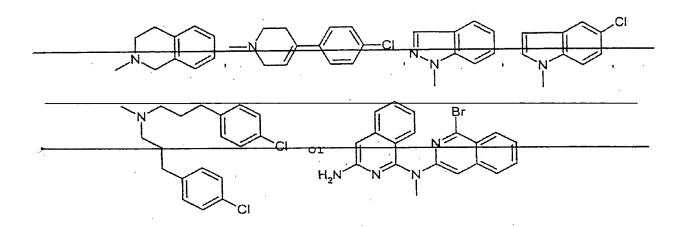
the group



or A, Z and R[†] together form the group

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m, n and o

stand for 0-3,

 R_a , R_b , R_c , R_d , R_e , R_f ,

stands for 1-6,

independently of one another, stand for hydrogen, C_{1-4} alkyl or the group =NR¹⁰, and/or R_a and/or R_b can form a bond with R_c and/or R_d or R_c can form a bond with R_e and/or R_f or up to two of radicals R_a - R_f can close a bridge with up to form a bridge of no more than 3 C-atoms each to form and said bridge is connected to R^1 or R^2 ,

X

stands for the group $=NR^9$ or =N-,

Y

stands for the group $-(CH_2)_p$,

p

stands for 1-4,

 \mathbb{R}^1

stands for unsubstituted aryl or heteroaryl, or for aryl or heteroaryl substituted one or more times with halogen;

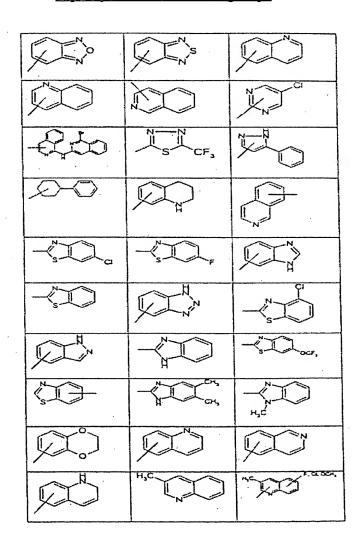
C₁₋₆ alkyl; or one or more times with halogen substituted C₁₋₆ alkyl or C₁₋₆ alkoxy; with the proviso that R⁺ naphthyl, biphenyl, phenyl, thiophenyl, furanyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl or isoquinolinyl that is

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unsubstituted or substituted in one or more places with halogen, C₁₋₆ alkyl or C₁₋₄-alkoxy, hydroxy, nitro, cyano or C₁₋₆-alkyl or C₁₋₆-alkoxy that is substituted in one or more places with halogen; or 5-chloro-2,3-dihydroindenyl, 2,3-dihydroindenyl, thienyl, 6-fluoro-1H-indol-3-yl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-oxadiazole, 6,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthyl or for one of the groups



 R^2

 \mathbb{R}^3

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wherein phenyl, substituted phenyl or naphthyl is not aryl directly bonded to $=NR^2$ in the meaning of A, stands for hydrogen or C_{1-6} alkyl or, with R_a-R_f from Z.

or to R¹, forms a bridge with up to 3 ring members with

 R_a - R_f from Z or to form R_f ,

stands for monocyclic or bicyclic aryl or heteroaryl that

is unsubstituted or optionally substituted in one or more

places with halogen, C_{1-6} alkyl, C_{1-6} alkoxy or hydroxy,

 R^4 , R^5 , R^6 , and R^7 , independently of one another, stand for hydrogen,

halogen, or C_{1-6} alkoxy, C_{1-6} alkyl or C_{1-6} carboxylalkyl that is unsubstituted or optionally substituted in one or

more places with halogen,

or R5 and R6 together form the group



 R^8 , R^9 , and R^{10} ,

Α

independently of one another, stand for hydrogen or C_{1-6} alkyl,

or an isomer or, pharmaceutically acceptable salt thereof, with the proviso that when A is $=NR^2$, X is $=NR^9$, $R^{2,4,6,7,9}$ is H, R^5 is Cl, W is O, Z=Y is $=CH_2$ -, and R^3 -is 4-pyridyl, then R^4 is not 3,4-methylendioxybenzyl.

2. (Amended) Compunds A compound of general formula I according to claim 1 in which

stands for the group $=NR^2$,

W stands for oxygen, sulfur, two hydrogen atoms or the

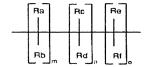
group =NR⁸, Page 12 of 39

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Z

stands for the group =NR¹⁰, =N- or -N(R¹⁰)-(CH₂)_a-, branched or unbranced C_{1-6} alkyl or the group



or A, Z and R1 together form the group

stand for 0-3, m, n, and o stands for 1-6, q $R_a R_b$, R_c , R_d , R_e and R_f , independently of one another, stand for hydrogen, C₁₋₄ alkyl or the group = NR^{10} stands for the group $=NR^9$ or =N-, X Y stands for the group $-(CH_2)_p$, stands for 1-4, p \mathbb{R}^1 stands for phenyl, pyridyl, 5-chloro-

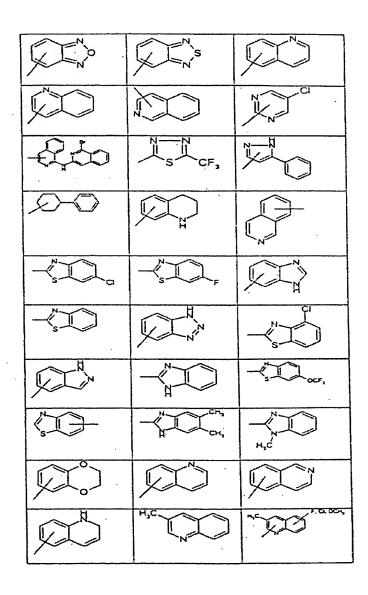
2,3-dihydroindenyl, 2,3-dihydroindenyl, thienyl,

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6-fluoro-lH-indol-3-yl, naphthyl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-oxadiazole, 6,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthyl or for phenyl or pyridyl that is substituted in one or more places with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy, halogen, or trifluoromethyl, or for the group



 \mathbb{R}^2

 \mathbb{R}^3

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whereby phenyl, substituted phenyl or naphthyl is not right in directly bonded to the =NR² group in the meaning of A

stands for hydrogen or C_{1-6} alkyl or with R_a - R_f from Z,

or to R¹, forms a bridge with up to 3 ring members with

R_a-R_f from Z or to form R_t,

stands for monocyclic or bicyclic aryl or monocyclic or

bicyclic heteroaryl that is unsubstituted or optionally substituted in one or more places with halogen, C_{1-6}

alkyl, C₁₋₆ alkoxy or hydroxy,

 R^4 , R^5 , R^6 and R^7 , independently of one another, stand for hydrogen,

halogen or $C_{1\text{-}6}$ alkoxy or $C_{1\text{-}6}$ alkyl that is unsubstituted or optionally substituted in one or more places with

halogen, or R5 and R6 together form the group

 R^{8} , R^{9} and R^{10} ,

independently of one another, stand for hydrogen or C_{1-6} alkyl,

as well as their isomers and salts or an isomer or pharmaceutically acceptable salt thereof.

3. (Amended) Compounds A compound of general formula I according to claim 1, in which

A stands for the group = NR^2 ,

W stands for oxygen, sulfur or two hydrogen atoms,

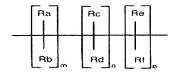
Z stands for the group = NR^{10} , =N, - $N(R^{10})$ -(CH_2)_q- or the

group

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or A, Z and R¹ together form the group

stand for 0-3,

m, n and o

X

stands for 1-6,

 R_a , R_b , R_c , R_d , R_e , R_f

independently of one another, stand

for hydrogen or methyl or the group $=NR^{10}$,

stands for the group $=NR^9$ or =N-,

stands for the group -CH₂-,

Y R^1

stands for phenyl, pyridyl, p-chlorophenyl, pmethylphenyl, p-methoxyphenyl, 5-chloro-2,3dihydroindenyl, 2,3-dihydroindenyl, thienyl, 6-fluoro-1H-indol-3-yl, naphthyl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-oxadiazole, 6,7-dimethoxy-1,2,3,4tetrahydro-2-naphthyl, or for phenyl or pyridyl that is substituted in one or more places with C₁-C₄ alkyl, C₁-

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C₄ alkoxy, hydroxy, halogen, trifluoromethyl, or for the group

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whereby phenyl, or substituted phenyl or naphthyl is not right in <u>directly bonded to</u> the =NR² group in the meaning of A,

 \mathbb{R}^2

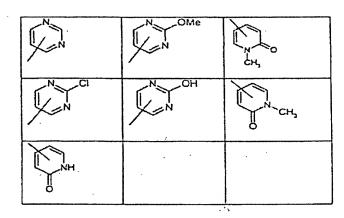
stands for hydrogen or methyl,

 \mathbb{R}^3

stands for pyridyl, or phenyl, or 1,2,3,4-

tetrahydronaphthyl that is substituted by hydroxy,

halogen, methyl or methoxy, or for the group



R⁵ and R⁶,

independently of one another, stand for hydrogen, halogen,

methyl, methoxy or trifluoromethyl,

 R^4 and R^7 ,

independently of one another, stand for hydrogen,

 R^9

stands for hydrogen,

 R^{10}

stands for hydrogen or methyl,

as well as their isomers and salts or an isomer or pharmaceutically acceptable salt thereof.

4. (Amended) Compounds A compound of general formula I according to claim 1, in which

Α

stands for the group $=NR^2$,

W

stands for oxygen,

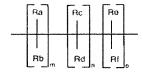
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Z

stands for the group =NR¹⁰, =N-, -N(R¹⁰)-(CH₂)_q- or the group



or A, Z and R¹ together form the group

m, n and o

stand for 0-3,

q

stands for 1-6,

 R_a , R_b , R_c , R_d , R_e , R_f ,

independently of one another, stand

for hydrogen or methyl or the group = NR^{10} ,

X

stands for the group $=NR^9$ or =N-,

Y

stands for the group -CH₂-,

 R^1

stands for phenyl, pyridyl, 5-chloro-2,3-dihydroindenyl,

2,3-dihydroindenyl, thienyl, 6-fluoro-1H-indol-3-yl,

naphthyl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-

oxadiazole or 6,7-dimethoxy-1,2,3,4-tetrahydro-2-

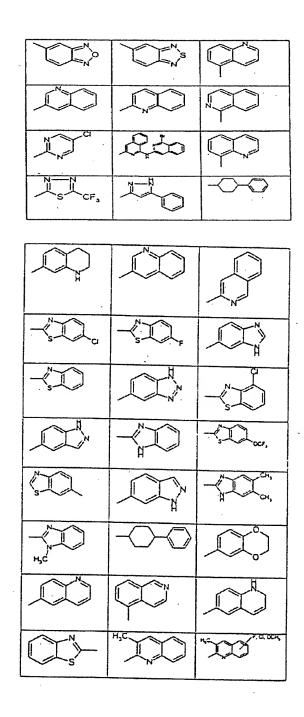
naphthyl or for a phenyl or pyridyl that is substituted in

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one more places with C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy, halogen, or trifluoromethyl, or for the group



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whereby phenyl, or substituted phenyl or naphthyl is not right in directly bonded to the =NR² group in the meaning of A,

R² stands for hydrogen or methyl,

R³ stands for pyridyl or for phenyl, pyridyl or 1,2,3,4tetrahydronaphthyl that is substituted in one or more places with hydroxy, halogen, methyl or methoxy, or

for the group

R⁵ and R⁶, independently of one another, stand for hydrogen, halogen,

methyl, methoxy, or trifluoromethyl,

 R^4 and R^7 , independently of one another, stand for hydrogen and halogen,

R⁹ stands for hydrogen,

R¹⁰ stands for hydrogen or methyl,

as well as their isomers and salts or an isomer or pharmaceutically acceptable salt thereof.

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5. (Amended) Compounds A compound of general formula I according to claim 1, in which

A stands for the group = NR^2 ,

W stands for sulfur,

Z stands for the group = NR^{10} , =N-, - $N(R^{10})$ -(CH_2)_q- or the group

or A, Z and R¹ together form the group

m, n and o stand for 0-3,

q stands for 1-6,

 R_a , R_b , R_c , R_d , R_e , R_f , independently of one another, stand for hydrogen or

methyl or the group = NR^{10} ,

X stands for the group = NR^9 or =N-,

Y stands for the group $-CH_2$ -,

R¹ stands for phenyl, pyridyl, 5-chloro-2,3-dihydroindenyl,

2,3-dihydroindenyl, thienyl, 6-fluoro-1H-indol-3-yl,

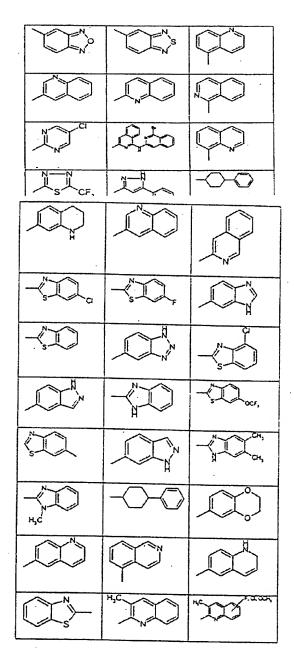
naphthyl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-

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oxadiazole or 6,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthyl or for phenyl or pyridyl that is substituted in one or more places with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy, halogen, or trifluoromethyl, or for the group



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whereby phenyl, or substituted phenyl or naphthyl is not right in bonded directly to the =NR² group in the meaning of A,

R² stands for hydrogen or methyl,

R³ stands for pyridyl or for phenyl, pyridyl or 1,2,3,4tetrahydronaphthyl that is substituted in one or more places with hydroxy, halogen, methyl or methoxy, or for the group

R⁵ and R⁶, independently of one another, stand for hydrogen, halogen, methyl, methoxy or trifluoromethyl,

R⁴ and R⁷, independently of one another, stand for hydrogen and halogen,

R⁹ stands for hydrogen,

R¹⁰ stands for hydrogen or methyl,

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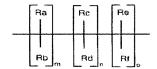
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6. (Amended) Compounds A compound of general formula I according to claim 1, in which

A stands for the group = NR^2 ,

W stands for two hydrogen atoms,

Z stands for the group =NR¹⁰, =N-, -N(R¹⁰)-(CH₂)_q- or the group



or A, Z, and R1 together form the group

m, n and o stand for 0-3, q stands for 1-6,

 R_a , R_b , R_c , R_d , R_e , R_f , independently of one another, stand

for hydrogen or methyl or the group = NR^{10} ,

X stands for the group = NR^9 or =N-,

Y stands for the group $-CH_2$ -,

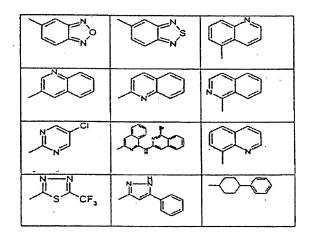
R¹ stands for phenyl, pyridyl, 5-chloro-2,3-dihydroindenyl,

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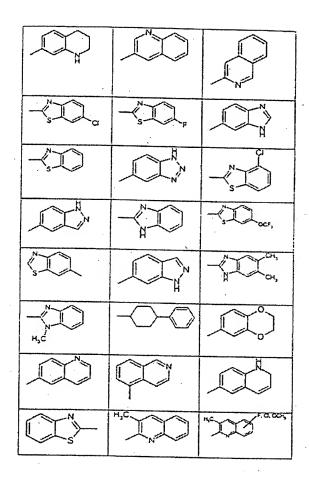
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2,3-dihydroindenyl, thienyl, 6-fluoro-1H-indol-3-yl, naphthyl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-oxadiazole or 6,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthyl or for a phenyl or pyridyl that is substituted in one or more places with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy, halogen, or trifluoromethyl, or for the group



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whereby phenyl, or substituted phenyl or naphthyl is not right in directly bonded to the $=NR^2$ group in the meaning of A,

stands for hydrogen or methyl,

stands for pyridyl or for phenyl, pyridyl or 1,2,3,4tetrahydronaphthyl that is substituted in one or more places with hydroxy, halogen, methyl or methoxy, or for the group

 R^2 R^3

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| , | Y | TN OMe | -3-5-5 |
|---|-------|-----------------------------------|--------|
| | \ | Z CI | N OH |
| | Z CI | N OMe | N OH |
| | N-CH, | $- \underbrace{\sum_{z}^{z}}_{z}$ | |

 R^4 and R^7 ,

independently of one another, stand for hydrogen, halogen,

methyl, methoxy or trifluoromethyl,

R⁵ and R⁶,

independently of one another, stand for hydrogen and halogen,

R9

stands for hydrogen,

 R^{10}

stands for hydrogen or methyl,

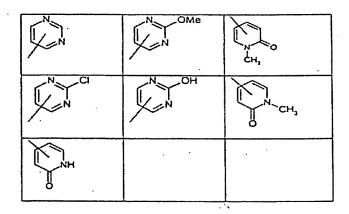
as well as their isomers and salts or an isomer or pharmaceutically acceptable salt thereof.

- 7. (Amended) A method of claim 11 for the treatment of tumors wherein said patient is suffering from a disease or condition mediated by VEGF which is a tumor, psoriasis, arthritis, hemangioma, angiofibroma, an eye diseases disease, neovascular glaucoma, a renal diseases disease, a fibrotic diseases disease, a mesangial-cell-proliferative diseases disease, arteriosclerosis, injuries an injury to the nerve tissue, and for inhibiting the reocclusion of vessels a vessel after balloon catheter treatment, in a vascular prosthetics prosthetic or after a mechanical devices are device is used to keep a vessels vessel open.
- 8. (Previously Amended) A pharmaceutical composition comprising a therapeutical effective amount of at least one compound according to claim 1 and a pharmaceutical acceptable carrier.

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- 9. canceled
- 10. canceled
- 11. (Previously Amended) A method of inhibiting the tyrosine kinase KDR and/or FLT, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 12. (Previously Amended) A method of producing a pharmaceutical preparation for enteral, parenteral and oral administration comprising mixing a compound of claim 1 with a suitable pharmaceutical carrier.
 - 13-15 (withdrawn from consideration)
 - 16. (New) A compound of claim 1, wherein
 - R³ stands for pyridyl, or phenyl, or 1,2,3,4tetrahydronaphthyl that is substituted by hydroxy, halogen, methyl or methoxy, or for the group



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17. (New) A compound of formula I

wherein

 \mathbf{A}

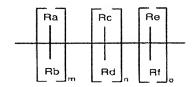
W

Z

stands for the group $=NR^2$,

stands for oxygen,

stands for the group



or A, Z and R1 together form the group

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m, n and o

stand for 0-3,

q

stands for 1-6,

 R_a , R_b , R_c , R_d , R_e , R_f

independently of one another, stand for

hydrogen, methyl, or the group = NR^{10} ,

X

stands for the group =NR⁹,

Y

stands for the group $-(CH_2)_p$,

p

stands for 1-4,

 R^1

stands for naphthyl, biphenyl, phenyl, thiophenyl, furanyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl or isoquinolinyl that is unsubstituted or substituted in one or more places with halogen, C_{1-6} alkyl or C_{1-4} -alkoxy, hydroxy, nitro, cyano or C_{1-6} -alkyl or C_{1-6} -alkoxy that is substituted in one or more places with halogen; or 5-

chloro-2,3-dihydroindenyl, 2,3-dihydroindenyl, thienyl,

6-fluoro-1H-indol-3-yl, 1,2,3,4-tetrahydronaphthyl, benzo-1,2,5-oxadiazole, 6,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthyl or for one of the groups

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| | | |

wherein phenyl, substituted phenyl or naphthyl is not directly bonded to $=NR^2$ in the meaning of A,

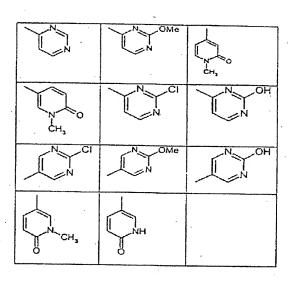
stands for hydrogen or methyl,

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 \mathbb{R}^3

stands for naphthyl, biphenyl, phenyl, thiophenyl, furanyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl or isoquinolinyl that is unsubstituted or substituted in one or more places with halogen, C_{1-6} alkyl or C_{1-6} -alkoxy or hydroxy, or for one of the groups



 R^4 , R^5 , R^6 , and R^7 ,

independently of one another, stand for hydrogen, halogen, or C_{1-6} alkoxy, C_{1-6} alkyl or C_{1-6} carboxylalkyl that is unsubstituted or substituted in one or more places with halogen, or R^5 and R^6 together form the group

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 R^8 , R^9 , and R^{10} ,

independently of one another, stand for hydrogen or $C_{\text{1-6}}$ alkyl,

or an isomer or, pharmaceutically acceptable salt thereof.